status and, importantly, at an ultrahigh dose, increased GSH and GSH/GSSG ratio to values comparable to those estimated in normotensive WKY rats. A greater increase in GSH/GSSG ratio also significantly correlated with a greater reduction in NF-κB activation and interstitial infiltrates.[2]

Normalization of redox state by an ultrahigh dose of Cand is particularly relevant if we consider that, as opposed to normotensive WKY rats, SHRs fail to upregulate the antioxidant defense as a compensatory mechanism to increased oxidative stress.

In line with the data of Chen *et al.*,[2] previous studies have documented infiltration of inflammatory lymphocytes and macrophages into the renal parenchyma of SHRs that can be reduced by the antioxidant melatonin.[9] This treatment also improved hypertension. It is likely that inflammatory cells present in the interstitium contribute to hypertension in SHRs by promoting local Ang II production and oxidative stress.

The anti-inflammatory effect of Cand has been previously investigated in SHRs in relation to hypertension-induced atherosclerosis in this model. Cand was shown to reduce the expression of vascular inflammatory cytokines to a greater extent than hypertensive triple therapy (hydralazine, hydrochlorothiazide, and reserpine) despite comparable blood pressure control.[12] Consistently, only Cand downregulated NF-κB p50 subunit precursor p105, suggesting that the anti-inflammatory effect of Cand is beyond blood pressure reduction and that AT1R partly contributes to NF-κB activation at least in blood vessels. In light of the paper by Chen *et al.*,[2] one may expect superior protective effects of ultrahigh dosage of Cand on vascular disease, independently of AT1R.

In patients with chronic kidney disease, a double-blind, randomized, prospective study has recently documented an additional antiproteinuric effect of an ultrahigh dose of Cand compared with a standard dose.[13] Whether the antiproteinuric effect translates into a slower rate of renal and cardiovascular end points has not been studied but can be speculated.

In the meantime, further experiments should prove the real benefit of ultrahigh dosage of Cand in comparison with standard dosage of Cand used alone or combined with an ACE inhibitor for chronic renal inflammation. This would support the rationale to test ultrahigh dosage of Cand, possibly targeted to oxidative stress, in the context of multiple drug treatment to induce remission of chronic kidney disease.

REFERENCES

1. Gill PS, Wilcox CS. NADPH oxidases in the kidney. *Antioxid Redox Signal* 2006; **8**: 1597–1607.
2. Chen S, Ge Y, Si J *et al.* Candesartan suppresses chronic renal inflammation by a novel antioxidant action independent of AT1R blockade. *Kidney Int* 2008; **74**: 1128–1138.
3. Benson SC, Pershadsingh HA, Ho CI *et al.* Identification of telmisartan as a unique angiotensin II receptor antagonist with selective PPARgamma-modulating activity. *Hypertension* 2004; **43**: 993–1002.
4. Morigi M, Macconi D, Zoja C *et al.* Protein overload-induced NF-kappaB activation in proximal tubular cells requires H(2)O(2) through a PKC-dependent pathway. *J Am Soc Nephrol* 2002; **13**: 1179–1189.
5. Benigni A, Corna D, Zoja C *et al.* Targeted deletion of angiotensin II type 1A receptor does not protect mice from progressive nephropathy of overload proteinuria. *J Am Soc Nephrol* 2004; **15**: 2666–2674.
6. Yoshioka T, Ichikawa I, Fogo A. Reactive oxygen metabolites cause massive, reversible proteinuria and glomerular sieving defect without apparent ultrastructural abnormality. *J Am Soc Nephrol* 1991; **2**: 902–912.
7. Brezniceanu ML, Liu F, Wei CC *et al.* Catalase overexpression attenuates angiotensinogen expression and apoptosis in diabetic mice. *Kidney Int* 2007; **71**: 912–923.
8. Zhan CD, Sindhu RK, Vaziri ND. Up-regulation of kidney NAD(P)H oxidase and calcineurin in SHR: reversal by lifelong antioxidant supplementation. *Kidney Int* 2004; **65**: 219–227.
9. Nava M, Quiroz Y, Vaziri N, Rodriguez-Iturbe B. Melatonin reduces renal interstitial inflammation and improves hypertension in spontaneously hypertensive rats. *Am J Physiol Renal Physiol* 2003; **284**: F447–F454.
10. Adler S, Huang H. Oxidant stress in kidneys of spontaneously hypertensive rats involves both oxidase overexpression and loss of extracellular superoxide dismutase. *Am J Physiol Renal Physiol* 2004; **287**: F907–F913.
11. Wilcox CS. Oxidative stress and nitric oxide deficiency in the kidney: a critical link to hypertension? *Am J Physiol Regul Integr Comp Physiol* 2005; **289**: R913–R935.
12. Sanz-Rosa D, Oubina MP, Cediel E *et al.* Effect of AT1 receptor antagonism on vascular and circulating inflammatory mediators in SHR: role of NF-kappaB/IkappaB system. *Am J Physiol Heart Circ Physiol* 2005; **288**: H111–H115.
13. Schmieder RE, Klingbeil AU, Fleischmann EH *et al.* Additional antiproteinuric effect of ultrahigh dose candesartan: a double-blind, randomized, prospective study. *J Am Soc Nephrol* 2005; **16**: 3038–3045.

see original article on page 1178

The importance of patient education in the treatment of chronic kidney disease

Chester Fox[1] and Linda S. Kohn

The article by Finkelstein and colleagues is a seminal work in helping us to understand the educational needs of pre–end-stage renal disease (pre-ESRD) patients. There are currently major deficits in patients' perceived knowledge of their options for ESRD care. The Canadian system, with its more integrated and multidisciplinary approach to care, does a better job of communicating these options to patients. African Americans are less likely to be aware of their options.

Kidney International (2008) **74**, 1114–1115. doi:10.1038/ki.2008.422

In this issue of *Kidney International*, Finkelstein and colleagues[1] point out that patients' perceived knowledge of their options for treatment in end-stage renal disease (ESRD) is limited. The authors also note that patient choice is the major factor in choosing a dialysis therapy as patients approach ESRD. Thus, patients' perceived lack of knowledge can have a major impact on treatment. This work is

[1]*Department of Family Medicine, University at Buffalo, Buffalo, New York, USA*
Correspondence: *Chester Fox, Department of Family Medicine, University at Buffalo, 462 Grider Street, Buffalo, New York 14215, USA.*
E-mail: chetfox@gmail.com

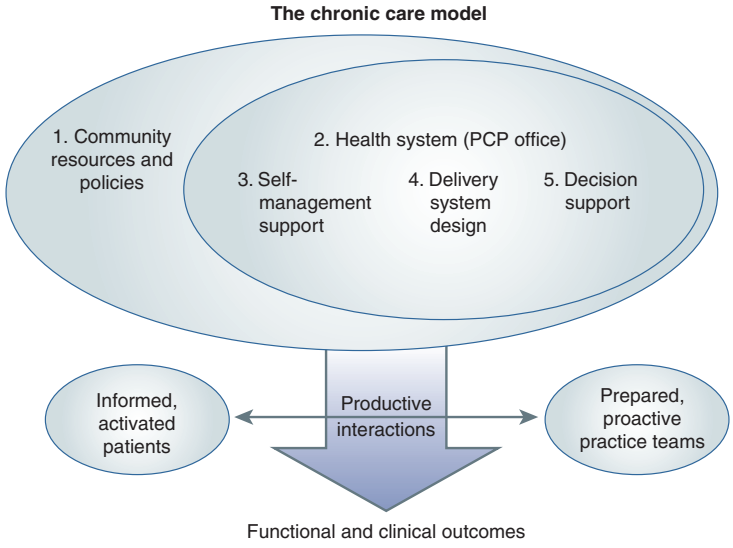

Figure 1 | The chronic care model developed by Ed Wagner and the Group Health Cooperative of Puget Sound. PCP, primary care physician.

particularly significant for two reasons. First, it demonstrates that it is not just lack of early referral to nephrologists that is causing this educational deficit. In this study, the average time under specialty care was 5.2 years. Second, the authors begin to define areas where future work is needed. This study has implications for how we both design and finance pre-ESRD care.

The chronic care model, as defined by Ed Wagner and colleagues, demonstrates that we need both prepared proactive practice teams and informed activated patients. A productive interaction is required between these two to improve clinical outcomes (Figure 1).[2] The article by Finkelstein *et al.*[1] begins to show us how we can do a better job informing patients. Having an adequate number of nephrologists is not enough. A multidisciplinary team—including dieticians, social workers, nurse educators, and pharmacists—and access to transplant surgeons are necessary to improve patient knowledge and understanding about progression of chronic kidney disease (CKD) and treatment options.

In addition, policy change that allows for reimbursement of these services, as well as for increased physician time per visit, is necessary if we are to have a truly informed patient. There is currently legislation before the United States Congress that would support this kind of initiative. Bills have been introduced in the Senate by Sens. Blanche Lincoln and Susan Collins (S. 432) and in the House by Reps. Mark Kirk and Jim McDermott (H.R. 1245) to establish a predialysis education benefit. In addition, the Kidney Care Quality and Education Act of 2007 (S. 691; H.R. 1193) includes a provision for a similar Medicare predialysis education benefit.

Finkelstein *et al.*[1] demonstrated that 35% of patients with pre-ESRD had no knowledge about any therapeutic modality for ESRD. Forty-three percent had no knowledge of hemodialysis, 57% of continuous ambulatory peritoneal dialysis, 66% of automated peritoneal dialysis, and 56% of transplantation. When patients were stratified by frequency of nephrology visits and stage of CKD, their knowledge about these treatment modalities improved. This suggests that only when the patient's condition worsens do knowledge and understanding of kidney disease improve, presumably because of increased contact with nephrologists. In addition, it was noted that in the Canadian system, where there is a more integrated approach to dialysis and CKD care, there was better perceived knowledge of treatment options. This again speaks to the importance of having the financial resources and necessary infrastructure for a multidisciplinary educational approach for patients with CKD.

This study also demonstrated that African Americans were less likely than either white or Asian patients to have adequate knowledge to make informed treatment decisions regarding hemodialysis, peritoneal dialysis, and transplantation. This is an important health disparity issue. It takes on even greater import because African Americans are much more likely to suffer from CKD.[3] Issues of health literacy and cultural competency need to be addressed as we design pre-ESRD care for this vulnerable population.

The study by Finkelstein *et al.*[1] has significant weaknesses. It should be noted that this is perceived knowledge, not actual knowledge. Also, the study had a very low response rate of 29.4%. Eighty-six percent of these responses were from Canadian patients, and less than 5% were from African American patients. In addition, most of the participating centers were prominent university medical centers in major cities in both Canada and the United States. The findings of this study may not be generalizable to small communities or to rural locales. These findings would need to be confirmed in larger studies and in different populations to be considered generalizable. Despite that, there is very little information about patient factors and knowledge in the current literature, which makes this a good first effort.

What can we learn from all this? First of all, we need to do a better job of understanding and addressing what our patients know about their treatment options regarding renal replacement thereapy. Second, it is important to have a multidisciplinary support team, including nurse educators, social workers, dieticians, and pharmacists, that is integral to this care. Finally, issues of health literacy and developing a culturally competent message need to be addressed to improve care to our African American patients and to reduce health disparities.

REFERENCES

1. Finkelstein FO, Story K, Firanek C *et al.* Perceived knowledge among patients cared for by nephrologists about chronic kidney disease and end-stage renal disease therapies. *Kidney Int* 2008; **74**: 1178–1184
2. Bodenheimer T, Wagner EH, Grumbach K. Improving primary care for patients with chronic illness: the chronic care model, Part 2. *JAMA* 2002; **288**: 1909–1914.
3. Coresh J, Selvin E, Stevens LA *et al.* Prevalence of chronic kidney disease in the United States. *JAMA* 2007; **298**: 2038–2047.